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10/809,312	03/24/2004	Lloyd A. Greene	070050.2897	6486

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EXAMINER	
KELLY, ROBERT M	

ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
11/19/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/809,312	GREENE ET AL.	
	Examiner	Art Unit	
	ROBERT M. KELLY	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,14-17,19 and 32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,14-17,19 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/5/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: (i) University of California v. Eli Lilly & Co. 119 F.3d 1559, 1567, 43 USPQ.2d 1398, 1405 (Fed. Cir. 1997); (ii) Festo Corporation v. Shoketsu Kinzoku Kogyo Kabushiki Co. LTD., 122 S.Ct. 1831 (2002).

DETAILED ACTION

Applicant's amendment and response of 8/5/08 has been entered

No amendments have been made.

Claims 1-11, 14-17, 19, and 32 are presently pending.

Claim Rejections - 35 USC § 112 – written description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 6-11, and 14-17 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims, as demonstrated by dependent claim 5, specifically imply that generas of inhibitors are broader than the antibodies, antisense RNAs and dominant negative inhibitors. Such includes, according to the specification, NGF and other proteins, small molecules, and antibodiotics, which inhibit, either directly or indirectly, the activity, expression, or degradation of the ATF5 protein.

However, no small molecule and no antibiotic is described in the specification or the art, which small molecule or antibiotic specifically, either directly or indirectly, inhibits the activity, expression or degradation of such ATF5.

Hence, the Artisan would not have understood Applicant to have been in possession of these specifically implied compounds.

Response to Argument – Written Description, breadth of inhibitors

Applicant's argument of 8/5/08 has been fully considered but is not found persuasive.

Applicant argues that the rejection is untimely, because there was an election of species on 5/24/07, which limits examination to dominant negative ATF5, and hence, the rejection should be withdrawn at this time (pp. 6-7, paragraph bridging).

Such is not persuasive. While the Examiner would love to ignore the increased subject matter which the Examiner is now considering, it is standard practice to rejoin species whenever the species are fully considered by the Examiner, and whenever the Examiner may decide on his/her own to rejoin the species. In essence, the typical response by an Applicant in response to a consideration of a non-elected species, however minimal, is that the Examiner constructively rejoined species because there was a full consideration, and the Office always holds such analysis up whenever a full consideration is made. It would be hard for the Examiner to argue that consideration was not full at this point. Hence, the species have been rejoined in a constructive manner, rather than formally.

Applicant argues that the specification provides a number of specific inhibitors of ATF5 which support the broader genera of Claim 1, and the fact that there could be additional species does not establish that support is insufficient (p. 7, paragraph 2).

Such is not persuasive. The claims specifically encompass antibiotics and small molecules which, either directly or indirectly inhibit the (i) activity, (ii) expression, and (iii)

degradation of ATF5, as is taught in the specification (e.g., paragraph 52 of the Application's publication: 2005/0164384). These genera are specifically encompassed by the broad claims.

Claim Rejections - 35 USC § 112—new matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 32 remains rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for reasons of record, as comprising new matter. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To wit, the substance of the rejection is that Applicant's original specification and claims only provides a demonstration of possession of eGFP as a fluorescent protein (e.g., paragraph 0014 of the Application Publication 2005/0164384 and original claims), however, present claim 32 contains the previously-amended language of encoding any fluorescent protein. Such necessarily obtains support from the specification which is one of obviousness, i.e., it would be obvious to use any protein which is fluorescent. However, as has been long made clear by the courts, obviousness-type support does not provide the proper demonstration of possession under the new matter type of written description rejection.

Response to Argument – New Matter, fluorescent protein

Applicant's argument of 8/5/08 has been fully considered but is not found persuasive.

Applicant argues that the Examiner does not have support for making the statement obviousness-type support does not support possession under the new matter type of written description rejection (pp. 7-8, paragraph bridging).

Such is not persuasive. Applicant's support is not found in the original filing, as the original filing only discusses eGFP, and never discusses the broader genera of a generic fluorescent protein. Hence, the Artisan would have to look elsewhere to find the other proteins and determine that they may serve the same function. Such is obviousness. Under new matter, however, Applicant is required to have demonstrated possession at the time of filing. In going to the Art, subsequent to the filing date to obtain support, the genera is necessarily not demonstrated as possessed at the time of filing. Applicant appears to be unaware of the patent law, hence, the following citation is proffered as an eloquent demonstration of the precedent is provided: *The Regents of the University of California v. Eli Lilly & Co.* 119 F.3d 1559, 1567, 43 USPQ.2d 1398, 1405 (Fed. Cir. 1997) (noting the court earlier held "a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention" and in this case holding disclosure of a species did not provide adequate written description of a genus).

Applicant argues, citing case law, that the requirement of possession only comes into play when the whole invention is directed to something distinct, and that *in haec verba* recitation of the genus is not required, as long as the Artisan would recognize that Applicants intended that the other species be useful (pp. 8-9, paragraph bridging).

Such is not persuasive. At its very core, Applicant's argument relies upon the decision that the Artisan recognize that Applicant intended the other species [of the newly claimed

genera] would be equally useful. Where in Applicant's specification and/or claims, as filed, does Applicant state that these other fluorescent proteins would be equally useful?

Applicant argues that the specification describes a sufficient number of species to represent the claimed genera, and therefore, it satisfies the written description requirement, thereby overcoming the new matter rejection (p. 9, last paragraph).

Such is not persuasive. The Examiner remains in disagreement with Applicant as to the requirements for new matter in an amended claim. While original claims may derive their support from the specification and prior art, an amended claim must derive sufficient support from the originally filed claims and specification.

Applicant argues that the instant Application provides provides the functional characteristic of eGFP which is equally applicable to the claimed genera of fluorescent proteins, and the Examiner has not provided any evidence to show that such is insufficient to lead the Artisan to the genus claimed. Finally, Applicant points to the disclosure in the specification that the Artisan, by reading the disclosure, would realize "that various changes in form and detail can be made without departing from the true scope of the invention in the appended claims", to argue that such does demonstrate possession of the claimed genera.

Such is not persuasive. The Examiner fails to understand what is meant by "the true scope of the invention in the appended claims". It would appear that the statement was filed with the original claims, and hence, would not apply to amended claims whatsoever. Further, the "true" scope is a theoretical term to which the Examiner is at loss to comment on. Overall, it would appear that such paragraph, however, is actually a general statement without substance. The claims are prosecuted to find the allowable subject matter, and Applicant may argue points,

or give up on the points at their will, but the true scope would appear to indicate that even if Applicant gave up on subject matter, they due coverage on such subject matter, because the true scope may be incongruent with a theoretically-allowed claim. Such is necessarily not allowed, as discussed in Festo Corporation v. Shoketsu Kinzoku Kogyo Kabushiki Co. LTD., 122 S.Ct. 1831 (2002). Given the mess which all these thoughts make of Applicant's statement, it would appear that such paragraph really has no discernable meaning in patent law.

Claim Rejections - 35 USC § 112 - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6, 8-11, 15, 17, and 19 remain, and Claims 1-5, 7, 14, and 16 are newly rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of inducing the differentiation of neural stem/progenitor cells *in vitro*, does not reasonably provide enablement for *in vivo* methods, or transplantation of the differentiated cells, and the breadth of inhibitors encompassed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims encompass methods of inducing/promoting the differentiation of neural stem/progenitor cells, by inhibiting ATF5 to reduce an activity of ATF5, and thereby promote differentiation. Such may be *in vivo* or *in vitro*, and the *in vitro* subsequently-differentiated cells may be transplanted into a subject, which may be human, an embryo, or into a subject with

nervous tissue degeneration. Dependent claims encompass additional contact with neurotrophic factors, specific differentiated cell types, GFP expression in the differentiated cell, and specific ATF5 inhibitors. Further, specific claims are drawn to similar methods under the preamble of treating nervous tissue degeneration.

Moreover, the methods for inducing differentiation *in vivo* and transplanting *in vitro* differentiated cells (herein discussed as "*ex vivo*" methods) are taught to be for the purpose of treating nervous tissue degeneration (e.g., p. 25, paragraph 0074, *et seq.*). Hence, these methods must be enabled for such therapies. Still further, the inhibitors of ATF5 are taught by the specification to encompass proteins, DNA, RNA, antisense, antibodies, antibiotics, drugs, etc., which can work directly or indirectly (e.g., p. 17, paragraph 0050, *et seq.*).

These claims are broad for the methods of *in vivo* differentiation and *ex vivo* therapies, as the breadth of inhibitors of ATF5 which decrease the activity of ATF5, as well as the breadth of administration methods encompassed.

The field of stem cell therapy for treating neurodenerative diseases is not very well fleshed out such that the Artisan could reasonably predict that any particular disorder could be treated, and further for any individual with the disorder. Pluchino, et al. (2005) Brain Research Reviews, 48: 211-19 teaches that the science is still in its infancy, with multiple art-recognized problems that must be overcome before applying widespread therapeutic applications of neural stem cell compositions to humans with neurogenerative disease/injury (e.g., p. 215, conclusion). The factors involved in the efficacy of such transplantation methods are not well understood.

In addition, Stanworth, et al. (2001) Clinical Medicine, 1(5): 378-82 teaches there are multiple issues impeding the widespread use of the combination of gene therapy and stem cells,

including lack of efficiency of gene transfer and vector design as well as regulatory issues (e.g., p. 381, col. 1, paragraph 3). Thomas, et al. (2003) Nature Reviews Genetics, 4: 346-58 teach that multiple hurdles must be overcome for viral vector administration, inlcuding potential immune response, limited understanding of integration potential into oncogenes, and the ability of animal studies to predict response in humans. Thomas discloses that the human response to viral based therapies are more variable than those observed in animal models and therefore, it is difficult to make solid predictions based on non-human trials (e.g., p. 356, col. 1, paragraph 2). Further, Thomas teaches that the predictability of individual response to inflammatory vectors remains a "substantial challenge" (e.g., Id.).

Further, stem cell therapy for neurodegenerative disease and trauma is not reasonably predictable. The lack of predictability is found in the areas of: efficacy of stem cell delivery to the area of degeneration, persistence in the disease area and proliferation control. Pluchino notes that while totipotent ES cells have been used in transplants, there is no consistent data on the use of ES cell derived, lineage restricted, neural cells (e.g., p. 213, paragraph 3). Further, Pluchino teaches that recent ES cell transplant studies have resulted in formation of heterologous tissue and teratomas at the site of administration (e.g., Id., paragraph 4). Further ES cell related issues include optimal sources of cells for transplant, optimal administration methods for the cells, and determination of differation state and persistence of the transplanted cells in the area to be treated (e.g., Id., p. 212, col. 1, last paragraph). Still further, it is not reasonably predictable that the properties of transplanted neural cells would remain after transplantation as *in vivo* animal models in which even adult differentiated cells displayed altered pathways of differentiation when they are transplanted into diseased animals versus healthy animals (e.g., pp. 213-14,

paragraph bridging). Efficacy of such stem cell pharmaceuticals is not reasonably predictable due to possible migration or dispersion of the stem cells to or from the degenerated area, especially in some diseases like Alzheimer's (e.g., Id.). In addition, any neural stem cells that are transplanted into a patient would be under the influence of a myriad of growth factors, hormones, and other molecules that would influence their differentiation fate and efficacy of treatment in any individual case (e.g., p. 214, last paragraph). Further, Gerlach, et al. (2002) Journal of Neurology, 249(Suppl. 3): III/33-35 cites multiple problems related to stem cell therapies including variation in therapeutic effect, side effects and the difficulty in using fetal or stem cell tissue (e.g., p. 34, col. 1, paragraph 3). The problems also lie in the unregulated proliferative potential of neural stem cells. Clinical evidence has shown that uncontrolled neural progenitor cells growth and differentiation in the brain of Parkinson's disease patients may result in death. In light of this, Gerlach suggests therapeutic implant of cells differentiated *in vivo* prior to transplant, but also cite the need to eliminate the possibility of uncontrolled proliferation and further suggest long-term preliminary studies in animals prior to widespread administration of such cells in human patients (e.g., p. 34, col. 2, paragraph 3).

Still further, the specific *in vivo* differenation and *ex vivo* therapies are argued against for several reasons, essentially amounting to the fact that for any specific disorder, specific cells are destroyed, degenerated, and affected, and the transplanted or differentiated cells must differentiate into or be transplanted into the tissue in the specific amounts and ratios to replace the specific cell type(s) that have been affected. Still further, these cells must actually replace the diseased cells in terms of not only presence, but also function.

To wit, while discussing stromal cells, the issues bought up by Bartley herein are applicable to the instant case, as the progenitors must be able to differentiate in the correct proportions and replace the damaged tissue. To wit, Bartley, et al. (2003) Expert Opin. Biol. Ther., 3(4): 541-49 provides an overview for stem cell therapy for cerebral palsy (TITLE) which will suffice to delineate some of the problems with such therapies. Bartley only recognizes that two methods of administration appear to be feasible for treatment of cerebral palsy, those of intravenous or direct injection (p. 542, col. 1, paragraph 4), neither of which, as will be shown below, is yet to be reasonably predictive of delivering enough cells to the site of action. In stating such, Bartley also recognizes that it is not reasonably predictable that any therapy can be effected with such cells injected into the vasculature, due to the permeability of the blood-brain barrier (Id.). Hence, on top of only two methods of administration being feasible to produce therapeutic effects, Bartley also recognizes that it is not necessarily reasonably predictable that vascular administration would produce a therapeutic effect. Next, with palsy, as with many diseases of the central nervous systems, patients have differing effects with regard to amounts of grey or white matter (and specific cell types and ratios of cell types) being lost, and therefore, the type of cell used to effect such therapy must be able to reasonably predictably differentiate into each of the cell types in the correct proportions (p. 542, col. 1, paragraph 5), and, in fact, it is not even reasonably predictable which or whether both need to be replaced in any particular instance of the disorder (Id.). Therefore, even for any subset of diseases of the CNS, it is not reasonably predictable which cells to replace in the first place, much less whether marrow stromal cells can do so for each cell type and in the correct proportions. Moreover, mere replacement of certain forms of cells may not effect a disease, as in palsy, where Bartley demonstrates that it is not

reasonably predictable that replacement of myelin, without replacement of the axons themselves, would facilitate any functional improvement (p. 542, col. 2, paragraph 2).

Bartley also indicates that the choice of cell type, stage of differentiation, and derivation are critical issues, indicating the specific stem cell may not be efficacious for any particular form of palsy, much less any disorder of the central nervous system (Id., paragraph 3). Further, for the cell type used in Bartley (MSCs), Bartley also provides numerous lines of evidence to indicate that marrow stromal cells can differentiate into various tissues and that such **may** be able to occur *in vivo* (p. 544, col. 1), but also there exists conflicting data (Id., paragraph 2). With regard to method of administration, Bartley again emphasizes that it would seem unlikely that intravenous injection would get enough cells to the site to effect treatment (p. 544, paragraph bridging columns). Further, Bartley questions the use of undifferentiated cells, and indicates that it is not reasonably predictable yet, requiring further experimentation, to determine the state of differentiation which should be applied in any particular treatment (p. 544, last paragraph). Furthermore, it is noted that even when these cell differentiate in some fashion, it is not clear whether such is the source of the therapeutic effect, or whether recovery is mediated by some other substance elaborated by the implanted cells (p. 545, col. 1, paragraph 2), and therefore, Applicant's requirement that the cells differentiate may actually not cause any therapeutic effect at all. Moreover, other results indicate that improvements in function may not be linked to the implantation of the cells themselves (Id., col. 2, paragraph 1), making the results suspect for any therapy associated with stromal cell therapy to the brain. Also, Bartley, even when a finding seems positive, indicates the need for further confirmation of the information before the data can be fully accepted (Id.).

Bartley also indicates that immune reactions may occur, which may be detrimental (Id., paragraph 2). This can further be interpreted that such immune reactions may kill any transplanted cells before they could effect therapy.

In conclusion, Bartley indicates that while the data is encouraging, extensive experimentation is still required before human treatment will be feasible (p. 545, col. 2, paragraph 2; p. 546, col. 1). Clearly, Bartley is indicating that somatic cell therapy with stromal cells is not reasonably predictable of therapy in humans at this point, which is after Applicant's filing date.

Still further, Savitz, et al. (2003) Journal of Cardiovascular Nursing, 18(1): 57-61, suggests that another disorder, stroke recovery, cannot be reasonably predicted with progenitor cells, as it is not known if the cells would actually replace the damaged cells, and in the proper proportions as well as the grafts would remain viable or die, which would require "**extensive investigation**" (e.g., p. 60, paragraph bridging columns). Further, extensive investigation would be required to yield useful data to draw practical information and make it reasonably predictalbe (last sentence).

Still further, in the case of Parkinson's disease, once the processes are lost that cross from the substantia nigra to the striatum, it would appear that the replacement with new processes is not reasonably predictable, even when living cells are present in the proper context, and encouraged to sprout new processes across the border (e.g., Bjorklund, et al. (2000) Brain Res., 886: 82-98, article in general) and further, even with the data presently available for treatment, the models utilized are not recognized by the Artisan to be reasonably predictive of treatment (e.g., INTRODUCTION, p. 83, col. 1, first full paragraph; pp. 89-90, paragraph bridging).

Lastly, while the Art and Applicant's specification demonstrate RNAi, antisense, dominant negative inhibitors, and antibodies, no demonstration is provided and no art is found of a small molecule or antibiotic that specifically inhibits ATF5 activity, expression, or increases its degradation specifically. Hence, the Artisan could not reasonably predict how to make such a molecule, which is specifically implied by the claims, as dependent claims claim the various ones shown, but the broad claim necessarily encompasses more, and the specification teaches small molecules and molecules that cause specific degradation (e.g., paragraph 50, et seq.).

In essence, it is clear that any particular transplant would require the correct cells in the correct proportions to be transferred to acheive a therapeutic effect in any disorder, but the amounts and proportions are not reasonably predictable, even when the evidence appears to suggest particular porportions/amounts, as it appears to not reasonably predictable in any case. Still further, simply differentiating into a particular type does not reasonably predict replacement of the damaged cell(s). Such replacements may not occur at all, or may occur to thwart normal cells in the damaged tissue, thereby not reasonably predicting any therapy. Still further, with damaged CNS tissue, it would not be reasonably predictable that any particular form of administration would allow the cells to reach the site of action due to the blood brain barrier, and it is further noted that other forms of administration to the peripheral nervous system are also known to be thwarted by the body's own systems, e.g., the liver would remove the cells from the blood system.

Still further, no base structures are known or reasonably predicted for the breadth of inibitors of activity implied by Applicant's claims, such that the Artisan could reasonably predict the embodiments specifically implied for the antibiotics and small molecules that inhibit the

activity of ATF5 or increase its degradation. Hence, the Artisan could not reasonably predict these molecules.

Applicant's specification and examples demonstrate the *in vitro* differentiation of neural progenitor cells, but fail to demonstrate any specific therapy, by transplant or *in vivo* administrations, and as such fails to overcome the various aspects considered non-enabled.

Hence, the Artisan would have to experiment with routes of administration for the various disorders, determine if the various administrations cause replacement of the damaged/affected cells in the proper proportions to treat the disease, and determine the breadth of specific inhibitors encompassed by screening compounds to determine which work. Such is considered undue as it amounts to inventing Applicant's claimed breadth for Applicant.

Hence, the claims are not enabled for that scope provided in the initial form paragraphs.

Response to Argument – Enablement

Applicant's argument of 8/5/08 has been fully considered but is not found persuasive.

Applicant argues that the Examiner is applying an improper standard to the *in vivo* therapy, with regard to safety and treatment efficacy issues associated with the therapy, because the claims are drawn to a methods of promoting differentiation (p. 12, last paragraph).

Such is partly persuasive. Applicant's sole purpose for these methods of differentiation are for therapeutic purposes, as the Examiner has previously stated in the rejection of 8/5/08, and as repeated above. Still further, as has been noted in the same rejection of 8/5/08, there are questions as to whether the cells would even predictably differentiate (e.g., pp. 8-9, paragraph bridging).

Applicant argues that, given the disclosure of Angelastro (2005) Journal of neuroscience, 25(15): 3889-99, the claims are enabled, because all that is required is differentiation of the cells (p. 13, paragraph 2).

Such is not persuasive. Angelastro 2005 details specific administrations and specific differentiations into astrocytes, which is not commensurate with Applicant's claimed subject matter, and in view of the Arguments the Examiner is making. Still further, which diseases does making more astrocytes cure? How does the Artisan know they will integrate in the correct proportions? The claims are simply not enabled for the sole described *in vivo* use.

Claim Rejections - 35 USC § 102 - anticipation

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 7, 12, 14, 16, and 18 remain rejected under 35 U.S.C. 102(b) as being anticipated by Angelastro, et al., (2000) Proceedings of the National of Academy of Science, USA, 276(15): 12190-121200 for reasons of record.

Applicant argues that the relevant definition in the specification is in paragraph 0145 wherein it is said that the "The ATF5 specific agent may be any agent reactive ATF5 protein or nucleic acid" (p. 13).

Such is not persuasive. The specific agent of the quoted paragraph appears to be limited to kits for assays for neural tumors. Moreover, the cited paragraph reference is open-ended, as it

"may be" these things, which necessarily implies that it may be other things. Still further, the specification specifically defines the agents to be much more, including indirect and direct inactivating, interfereing with, or downregulating CRE-binding of ATF5 (paragraph 0050), and may be, specifically, NGF (paragraph 0053). Arguing conflicting "definitions" is not a productive manner in which to proceed, and is actually not considered persuasive in the courts. Hence, Applicant's argument is no longer addressed.

Response to Argument – Anticipation, Angelastro 2000

Applicant's argument of 8/5/08 has been fully considered but is not found persuasive.

Applicant argues that the Examiner cannot consider Angelastro at this time because there was an election of species which precludes use of other members of the genera of the broad claim, except for dominant negative ATF (p. 14, paragraph 2).

Such is not persuasive. The Examiner, as is stated above, has fully considered the breadth of the claimed inhibitors already, which may be done at the Examiner's perogative. In addition, once considered, it cannot suddenly be withdrawn.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT M. KELLY whose telephone number is (571)272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert M Kelly/
Primary Examiner, Art Unit 1633